A genome-wide RNAi screen in *Drosophila* identifies novel regulators of the Ca\(^{2+}\)/calcineurin/ NFAT signalling pathway

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The NFAT family of Ca\(^{2+}\)-regulated transcription factors has a critical role in vertebrate development and function. In resting cells, NFAT proteins are heavily phosphorylated and reside in the cytoplasm; upon stimulation they are dephosphorylated by the calmodulin-dependent phosphatase calcineurin and translocate to the nucleus. NFAT proteins are not represented in invertebrates, but the pathways regulating their subcellular localization -- Ca\(^{2+}\) homeostasis, Ca\(^{2+}\) influx, calcineurin and NFAT kinases -- are strongly conserved across species. Using a genome-wide RNAi screen in *Drosophila*, we have identified several previously unsuspected modulators of NFAT function: *Drosophila* and human STIM proteins which are powerful regulators of Ca\(^{2+}\) influx in response to depletion of Ca\(^{2+}\) stores; DYRK, a kinase that directly phosphorylates a conserved motif in the NFAT regulatory domain and deactivates NFAT; and other candidates that affect diverse aspects of Ca\(^{2+}\) signalling and NFAT regulation. Thus genome-wide RNAi screening in *Drosophila* can be successfully used to cross evolutionary boundaries and identify novel regulators of a transcription factor that is expressed only in vertebrates.

References

